Effect of hyperventilation on regional cerebral blood flow in head-injured children

Peter Skippen, FANZCA; Michael Seear, FRCP; Ken Poskitt, FRCP; John Kestle, FRCSC; Doug Cochrane, FRCSC; Gail Annich, FRCP; Jeffrey Handel, MRCP

Objectives: To study cerebral blood flow and cerebral oxygen consumption in severe head-injured children and also to assess the effect of hyperventilation on regional cerebral blood flow.

Design: Prospective cohort study.

Setting: Pediatric intensive care unit at a tertiary-level university children's hospital.

Patients: Twenty-three children with isolated severe brain injury, whose admission Glasgow Coma Scores were <8.

Interventions: $Paco_2$ was adjusted by altering minute ventilation. Cerebral metabolic measurements were made at three levels of $Paco_2$ (>35, 25 to 35, and <25 torr [>4.7, 3.3 to 4.7, and <3.3 kPa]) after allowing 15 mins for equilibrium.

Measurements and Main Results: Thirty-eight studies (each study consisting of three sets of measurements at different levels of $Paco_2$) were performed on 23 patients. At each level of $Paco_2$, the following measurements were made: xenon-enhanced computed tomography scans; cerebral blood flow; intracranial pressure; jugular venous bulb oxygen saturation; mean arterial pressure; and arterial oxygen saturation. Derived variables included: cerebral oxygen consumption; cerebral perfusion pressure; and oxygen extraction ratio. Cerebral blood flow decreased below normal after head injury (mean 49.6 ± 14.6 mL/min/100 g). Cerebral oxygen consumption decreased out of proportion to the decrease in cerebral blood flow; cerebral oxygen consumption was only a third of the normal range (mean 1.02 ± 0.59 mL/min/100 g). Neither cerebral blood flow nor cerebral oxygen consumption showed any relationship to time after injury, Glasgow Coma Score at the time of presentation, or intracranial pressure. The frequency of one or more regions of ischemia (defined as cerebral blood flow of <18 mL/min/100 g) was 28.9% during normocapnia. This value increased to 73.1% for $Paco_2$ at <25 torr.

Conclusions: Severe head injury in children produced a modest decrease in cerebral blood flow but a much larger decrease in cerebral oxygen consumption. Absolute hyperemia was uncommon at any time, but measured cerebral blood flow rates were still above the metabolic requirements of most children. The clear relationship between the frequency of cerebral ischemia and hypocarbia, combined with the rarity of hyperemia, suggests that hyperventilation should be used with caution and monitored carefully in children with severe head injuries. (Crit Care Med 1997; 25:1402–1409)

KEY WORDS: head injury; hyperventilation; cerebral blood flow; jugular venous oximetry; xenon computed tomography scan; cerebral ischemia

In health, cerebral blood flow is closely regulated by the cerebral metabolic rate of oxygen consumption ($CMRO_2$). The relationship is described by the Fick equation (1, 2) (Eq. *1*, Appendix). Since the ratio between $CMRO_2$ and cerebral blood flow is constant over a wide range, the arterial-jugular venous oxygen content difference ($C(a\text{-}j)O_2$) usually remains stable at about 6 mL/100 mL of blood (1, 2).

After serious head injury in adults, numerous studies have shown that $CMRO_2$ decreases predictably to less than half the normal resting level of about 3 mL/min/100 g of tissue (3). The response of cerebral blood flow to head injury is more complex (4). In some patients, coupling is preserved; cerebral blood flow decreases with the reduction in $CMRO_2$ so that $C(a\text{-}j)O_2$ remains constant. If coupling is lost, cerebral flow is no longer governed by metabolic requirements. Flow may increase, causing cerebrovascular engorgement with a decrease in $C(a\text{-}j)O_2$, or flow may decrease excessively, leading to ischemia and an increase in $C(a\text{-}j)O_2$ as oxygen extraction increases (5). The situation is further complicated by the demonstration that areas of hypoperfusion and hyperperfusion may often exist within the same patient (6).

Ischemic brain injury is a common *post mortem* finding in adults dying of head injury (7). Hypoxic-ischemic damage at the time of injury is important, but it was suspected for years that cerebral hypoperfusion in the first few hours after injury contributed to the brain injury (8). Recent technological advances have allowed early flow measurements to be made, confirming that the adult response to head injury is frequently early cerebral hypoperfusion followed by mild hyperemia after 12 to 24 hrs (8, 9).

The situation in children is less clear. Earlier work by Bruce et al. (10, 11) suggested that the response of children to head injury was, more usually, early cerebral hyperemia leading to an increase in cerebral blood

From the Departments of Intensive Care (Drs. Skippen, Seear, Annich, and Handel), Radiology (Dr. Poskitt), and Neurosurgery (Drs. Kestle and Cochrane), British Columbia's Children's Hospital, Vancouver, BC, Canada.

Supported, in part, by a grant from British Columbia's Children's Hospital Telethon Fund.

Address requests for reprints to: Dr. Peter Skippen, Intensive Care Unit, British Columbia's Children's Hospital, 4480 Oak Street, Vancouver, BC V6H 3V4, Canada.

volume and a consequent increase in intracranial pressure. Their recommendations of early elective hyperventilation and avoidance of mannitol are still widely cited, despite the fact that the recommendations were based on measurements in only six children (12). More recent studies (13, 14) have shown that the cerebral metabolic and vascular responses to head injury in children are less predictable than previously claimed and have also raised concerns about the safety of routine hyperventilation.

Hyperventilation causes cerebral vasoconstriction, probably in response to induced cerebrospinal fluid alkalosis (15). The effect wears off in a few hours, probably due to cerebrospinal fluid buffering (16). Global vasoreactivity is usually preserved, despite serious head injury (17), although regional reactivities may vary widely in a given patient (18). Questions about the risk of inducing cerebral ischemia were raised shortly after hyperventilation was introduced into clinical practice (19). There is some justification for these concerns: the only controlled trial of the therapy showed slower recovery times among the hyperventilated group (20), while other studies (6, 21) demonstrated clinically important regional ischemia during periods of hyperventilation. Consequently, early routine hyperventilation is not currently recommended in the adult literature (22).

In view of the limited pediatric information, our study had two objectives: a) to study the cerebral metabolic and vascular responses to severe head injury in children; and b) to assess the effect of hyperventilation on regional cerebral blood flow rates.

MATERIALS AND METHODS

Patient Population. We studied 23 children admitted to our pediatric intensive care unit with isolated head injuries and a Glasgow Coma Score of <8. Patient characteristics are outlined in Table 1.

The study was approved by the Ethics Committee of the University of British Columbia. Written parental or guardian consent was obtained for all patients.

Patient Management. As far as possible, a standardized management protocol was used for each child. All patients were intubated and mechanically ventilated. Unless otherwise indicated, $Paco_2$ was maintained at 35 to 40 torr (4.7 to 5.3 kPa). Intracranial pressure was continuously measured in all children using an intraventricular catheter that was usually inserted at the bedside under sedation and local anesthesia. Volatile anesthetic agents were avoided in any child requiring general anesthesia. The patient's head was positioned carefully to avoid venous compression. Sedation was achieved with infusions of morphine and midazolam. Hyperthermia was treated with a cooling blanket. Paralysis was only used to prevent shivering due to the cooling blanket or for uncontrollable intracranial pressure. Phenytoin was used for seizure control where indicated. Early feeding was instituted via nasogastric tube or nasoduodenal tube. In addition, all patients were monitored with intra-arterial and jugular venous catheters.

If the intracranial pressure remained increased above 15 mm Hg for >5 mins, the intraventricular catheter was opened to drain for 5 mins. Osmotic diuretic agents were administered if the pressure remained consistently increased despite free cerebrospinal fluid drainage. Mild hyperventilation was used if the pressure still remained high.

The management of children whose intracranial pressure remained increased, despite this protocol, was modified to suit the particular patient but generally consisted of the following treatments: a) paralysis and cooling to achieve a core temperature of <35°C; b) cautious hyperventilation aiming to keep the cerebral oxygen extraction ratio at <30%; c) cardiovascular support (23) using fluid boluses and inotropes, aiming to keep cerebral perfusion pressure at >50 mm Hg for patients <12 yrs of age and at >60 mm Hg for patients >12 yrs of age. More aggressive hyperventilation, combined with osmotic therapy and support of cerebral perfusion pressure, was instituted for acute emergencies, such as dilation of a pupil. This intervention was usually followed by an urgent computed tomography (CT) scan. Neither high-dose phenobarbitone therapy nor corticosteroids were used in any child.

Table 1. Patient (pt) characteristics

No. of pts studied	23 (12 boys, 11 girls)
Mean age (yr)	11 (range 3 mos to 16 yrs)
Mechanism of injury	19 MVAs, 4 nonaccidental injuries
Postresuscitation GCS[a]	
GCS 3	2 pts (1 bilateral fixed dilated pupils)
GCS 4	11 pts (1 unilateral fixed dilated pupil)
GCS 5	2 pts
GCS 6	1 pt
GCS 7	7 pts
Traumatic Coma Data Bank CT Scan Diagnosis[b]	
Mass lesion, intra- or extracerebral	5 pts
Diffuse swelling without midline shift	3 pts
Diffuse swelling with midline shift	1 pt
Small parenchymal hemorrhage	6 pts
Other abnormality	8 pts
Normal CT scan	0 pt

MVAs, motor vehicle accidents; GCS, Glasgow Coma Score; CT, computed tomography. [a]No patients were hypotensive before admission; [b]see Eisenberg et al (37).

Table 2. Outcome of 23 patients at 6 months

Admission GCS	Glasgow Outcome Score				
	Good	Moderate	Severe	Vegetative	Dead
7	3	2	1	—	1
6	—	1	—	—	—
5	2	—	—	—	—
4	1	2	4	4	—
3	1	—	—	1	—

GCS, Glasgow Coma Score; —, no patients (0).

Study Design. Thirty-eight studies were performed on 23 patients. Eighteen of these studies were made within the first 24 hrs after injury. Each study consisted of a set of three cerebral blood flow studies at different levels of $Paco_2$. The initial scan was performed at a $Paco_2$ of 35 to 40 torr (4.7 to 5.3 kPa). Minute ventilation was then increased to produce a stepwise reduction in $Paco_2$ to 25 to 35 torr (3.3 to 4.7 kPa) and lastly to <25 torr (<3.3 kPa). Ventilator changes were initially monitored by measurement of end-tidal CO_2. At equilibrium, the true $Paco_2$ was checked by an arterial gas sample. Fifteen-minute equilibration periods were allowed after ventilator changes. At each level of $Paco_2$, measurements were made of cerebral blood flow, intracranial pressure, jugular venous bulb oxygen saturation, mean arterial pressure, and arterial oxygen saturation. Some patients were not stable enough to allow a full set of three cerebral blood flow studies. A final total of 96 measurements was made.

Cerebral Blood Flow Measurements. Global and regional cerebral blood flows were measured by xenon-enhanced CT (24). After a baseline cranial CT study, three 5-mm axial images were chosen to maximize the sampling of the brain stem, cerebellum, basal ganglia, cortex, and any injured brain. A mixture of 28% xenon, 30% to 50% oxygen and nitrogen was administered over 3.5 mins using a gas delivery system and measurement console (Anzai, Yokogawa Electric Corporation, Tokyo, Japan). The first image was obtained 30 secs after starting gas inhalation. Further scans were performed each minute, for a total of 5 mins, to obtain images at the washin, plateau and washout phases of the study. The initial axial levels chosen were used for all repeat measurements. All patients were paralyzed and sedated throughout the study. All changes in $Paco_2$ were stepwise reductions.

Measurements of Arterial-Jugular Venous Oxygen Content Difference-Cerebral Metabolic Rate of Oxygen Consumption. Each child was monitored with an indwelling jugular venous bulb catheter inserted via a retrograde approach so that the tip was in the jugular bulb. The position was confirmed by a lateral cervical radiograph (25). There was no routine for selecting the side of catheter insertion. During measurement of cerebral blood flow, arterial and jugular venous bulb blood samples were drawn and sent to the laboratory for determination of oxygen saturation (by cooximeter) and oxygen partial pressure. The cross-brain arterial venous oxygen content difference ($C(a\text{-}j)o_2$, mL/100 mL) was calculated from Equation *2* (Appendix). The cerebral metabolic rate for oxygen ($CMRO_2$, mL/min/100 g) was then calculated from simultaneous measurements of $C(a\text{-}j)o_2$ and cerebral blood flow using Equation *1* (Appendix).

Other Calculated Variables. Cerebral perfusion pressure, CO_2 vasoreactivity, and cerebral oxygen extraction ratio were also derived. Cerebral perfusion pressure was calculated as the difference between mean arterial pressure and intracranial pressure (Eq. *3*, Appendix). CO_2 vasoreactivity expresses the percentage change in cerebral blood flow per torr change in $Paco_2$ and was calculated using Equation *4* (Appendix).

The cerebral oxygen extraction ratio is calculated from Equation *5* (Appendix).

Choice of Normal Values. The interpretation of measured values depends on their comparison with accepted normal ranges. Unfortunately, the available information is limited and difficult to interpret. For instance, values cited for normal cerebral blood flow range from 106.4 ± 9.9 mL/min/100 g in unsedated children (26) to 31 mL/min/100 g in unsedated premature-born infants (27). We used data from Settergren et al. (28) for the normal values, which were based on the only large study of cerebral metabolism in anesthetized children (cerebral blood flow of 65.0 ± 16.2 mL/min/100 g, $C(a\text{-}j)o_2$ of 4.86 ± 1.61 mL/min/100 g, and $CMRO_2$ of 3.02 ± 1.0 mL/min/100 g). These values compare well with the normal values in the original work by Kety and Schmidt (29) on unsedated adults, and have also been used as the basis of comparison for two large studies (14, 30) of head-injured children.

Defining the lowest acceptable limit of cerebral blood flow is also difficult. It has been shown that regional cerebral flows of 8 to 16 mL/min/100 g are associated with loss of cellular function and absence of synaptic transmission (31). Cold (21) defined cerebral oligemia as a regional cerebral blood flow of 15 to 20 mL/min/100 g. In keeping with an earlier study by Bouma et al. (9), we defined cerebral ischemia as any regional cerebral blood flow of <18 mL/min/100 g.

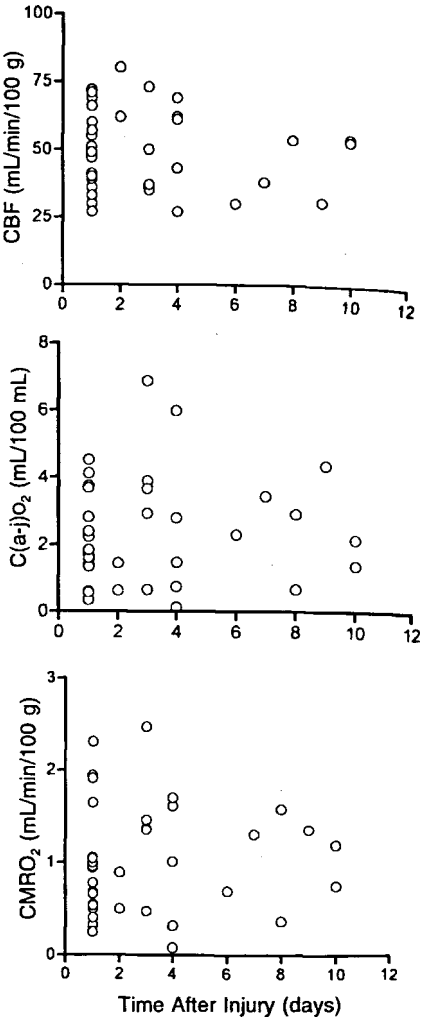

Figure 1. Simultaneous measurements of cerebral blood flow (*CBF*) (*top*, mean 49.6 ± 14.6 mL/min/100 g), arterial-jugular venous oxygen content difference ($C(a\text{-}j)o_2$) (*middle*, mean 2.30 ± 1.56 mL/min/100 g), and cerebral metabolic rate of oxygen consumption ($CMRO_2$) (*bottom*, mean 1.02 ± 0.59 mL/min/100 g) plotted against time after initial injury. All measurements were made at $Paco_2$ values of 35 to 40 torr (4.7 to 5.3 kPa).

Statistics. All numbers are expressed as mean ± SD. The linear line of best fit through multiple data points was calculated by the least squares method. Comparisons between interval data were made by unpaired *t*-test. Comparisons between frequency data were

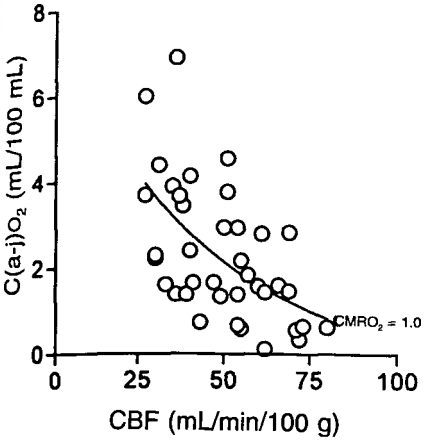

Figure 2. Cerebral blood flow (*CBF*) measured at $Paco_2$ values of 35 to 40 torr (4.7 to 5.3 kPa) plotted against simultaneous measurements of arterial-jugular venous oxygen content difference (*C(a-j)o_2*). The *line of identity*, which was calculated by the Fick equation and which represents cerebral metabolic rate of oxygen consumption (*$CMRO_2$*) = 1.0 mL/min/100 g, is superimposed on the graph.

made with Fisher's exact test. A $p < .05$ was considered significant.

RESULTS

Outcome. All patients received a follow-up examination 6 months after discharge from the intensive care unit. Outcome was assessed using the five-point Glasgow Outcome Score (good, moderate, severe, vegetative, dead) (32). The results of outcome compared with initial Glasgow Coma Score are summarized in Table 2. Overall, the outcomes were as follows: 12 (52.2%) of the patients had a good or moderate outcome; 10 (43.5%) of the patients had conditions that were severe or vegetative; and one child (4.3%), who had been making a moderately good recovery, died of a ruptured traumatic cerebral aneurysm.

Variation of Cerebral Blood Flow and Cerebral Metabolic Rate of Oxygen Consumption With Time After Injury. Researchers (3, 13) have corrected cerebral blood flow measurements to a normalized $Paco_2$ of 34 torr (4.5 kPa), assuming a 3% vasoreactivity. We chose not to do this correction because of the wide variation in CO_2 vasoreactivity (mean 2.7%/mm Hg, range 7.1 to –2.3%/mm Hg) that we have discovered. In all figures, we have displayed uncorrected cerebral blood flow and $CMRO_2$ measurements made in the $Paco_2$ range of 35 to 40 torr (4.7 to 5.3 kPa). Measurements made at lower $Paco_2$ levels were only used to assess the change of cerebral blood flow with hyperventilation. Figure 1 shows how cerebral blood flow, C(a-j)o_2, and $CMRO_2$ vary with time after injury. There was no apparent trend between any of the variables and time. Linear regression lines were not computed for Figure 1 since the graphs represent pooled repeat measurements. Group mean values were calculated and are given in the figure legend. Although the mean global cerebral blood flow

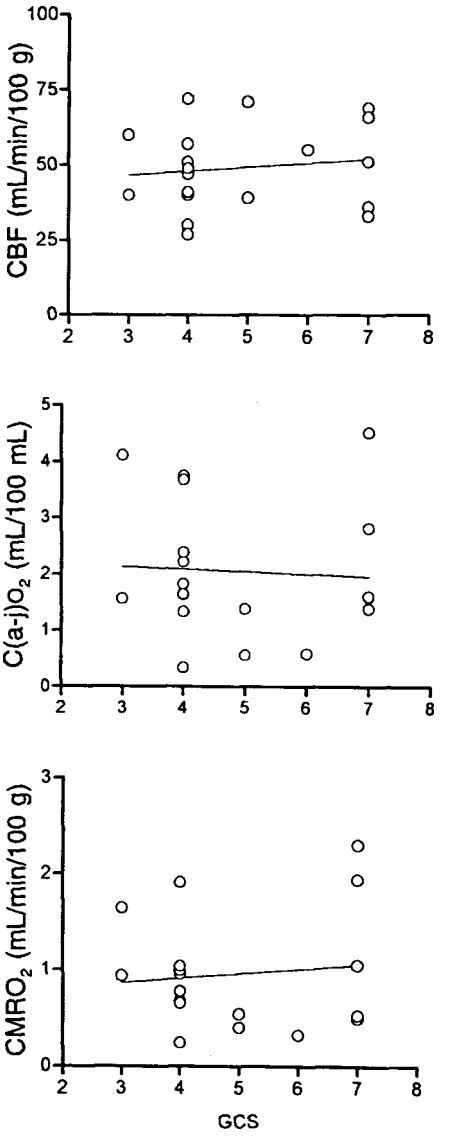

Figure 3. Simultaneous measurements of cerebral blood flow (*CBF*), arterial-jugular venous oxygen content difference (*C(a-j)o_2*), and cerebral metabolic rate of oxygen consumption (*$CMRO_2$*) plotted against admission Glasgow Coma Score (*GCS*). All measurements were made within 24 hrs of head injury. All R values <0.1.

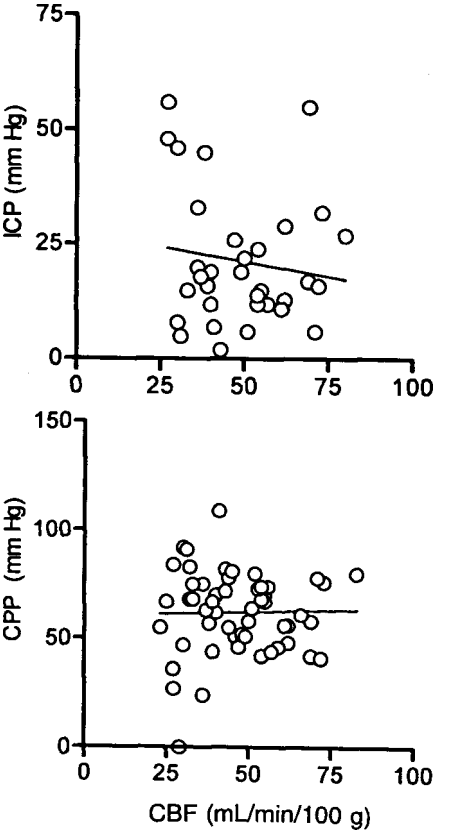

Figure 4. Cerebral blood flow (*CBF*) plotted against simultaneously measured intracranial pressure (*ICP, top*) and calculated cerebral perfusion pressure (*CPP, bottom*). All measurements were made at $Paco_2$ values of 35 to 40 torr (4.7 to 5.3 kPa). All R values <0.1.

rate in our study was significantly lower than that rate reported by Settergren et al. (28) (49.6 ± 14.6 mL/min/100 g vs. 65.0 ± 16.2 mL/min/100 g, $p < .05$), the spread of values was generally within the lower range cited by Settergren et al. However, our values for C(a-j)o_2 (2.30 ± 1.56 mL/100 mL) and $CMRO_2$ (1.02 ± 0.59 mL/min/100 g) were reduced out of proportion to the reduction in cerebral blood flow. The C(a-j)o_2 and $CMRO_2$ values were both less than half those values reported by Settergren et al. (28) (4.86 ± 1.61 mL/100 mL and 3.02 ± 1.0 mL/min/100 g, respectively, both $p < .001$). The relationship between global cerebral blood flow and C(a-j)o_2 is demonstrated in Figure 2. The line of identity representing $CMRO_2$ = 1.0 mL/min/100 g (calculated by the Fick equation) is superimposed on the graph.

Variation of Cerebral Blood Flow With Glasgow Coma Scale, Intracranial Pressure, and Cerebral Perfusion Pressure. Cerebral blood flow, C(a-j)o_2,

and $CMRO_2$ were measured within 24 hrs of the initial head injury in 18 children. The results are plotted against admission Glasgow Coma Score (Fig. 3). There was no relationship between any of the variables and the patient's initial neurologic presentation. In addition, there was no relationship between cerebral blood flow and intracranial pressure or cerebral perfusion pressure measured at any time (Fig. 4).

Variation of Cerebral Blood Flow With $Paco_2$ and Frequency of Regional Ischemia. The response of global cerebral blood flow to variations in $Paco_2$ was preserved in most patients, despite head injury. Figure 5 (*top*) is a composite of all 38 sets of cerebral blood flow measurements made at different levels of Pco_2. The calculated CO_2 vasoreactivity was 2.7%/mm Hg, but the range varied from 7.1 to –2.3%/mm Hg. The frequency of regional cerebral ischemia increased significantly with hyperventilation. However, even during normocapnia, 28.9% of patients had one or more areas of regional cerebral blood flow at <18 mL/min/100 g. In addition, two patients developed global ischemia after hyperventilation. The frequency of global ischemia increased to 73.1% at a $Paco_2$ of <25 torr (3.3 kPa) (Fig. 5, *bottom*). Xenon-enhanced CT scanning provided clear visual evidence of the potential risks of unmonitored hyperventilation. In some patients, small changes in $Paco_2$ were accompanied by marked decreases in cerebral blood flow (Fig. 6).

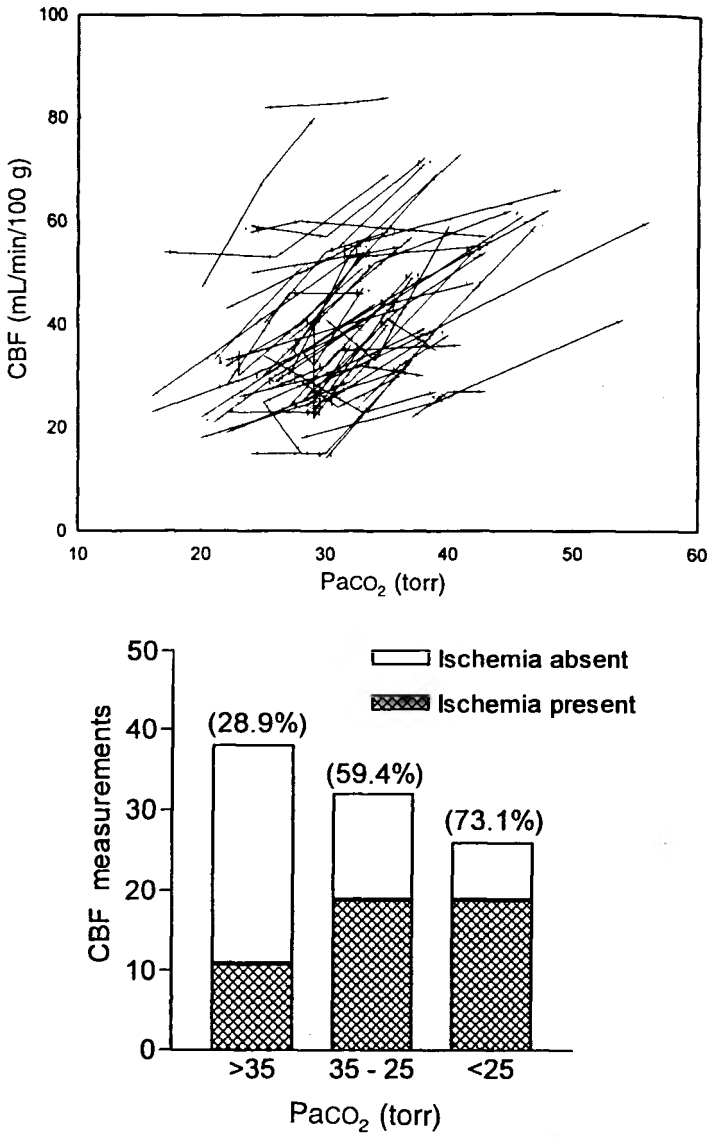

Figure 5. *Top:* 38 sets of cerebral blood flow (*CBF*) measurements made after alterations in $Paco_2$. Mean CO_2 vasoreactivity was 2.7%/mm Hg (range 7.1 to –2.3%/mm Hg). *Bottom:* The frequency of one or more areas of cerebral ischemia (cerebral blood flow [*CBF*] rates at <18 mL/min/100 g) in a child's computed tomography scan plotted against the $Paco_2$ range at the time of measurement. *Numbers on top of bars* indicate percentage of ischemia.

DISCUSSION

We measured cerebral blood flow, $C(a\text{-}j)o_2$, and $CMRO_2$ in 23 children to assess their cerebral metabolic and vascular responses to head injury. In addition, we examined the relationship between cerebral blood flow and $Paco_2$ to study the frequency of cerebral ischemia during periods of hyperventilation.

The original work of Bruce et al. (10), which concluded that early cerebral hyperemia was common in head-injured children, was investigated by two large pediatric studies (13, 14). Muizelaar et al. (13) stated that early cerebral hyperemia was common in head-injured children when compared with a normal value of 44.1 mL/min/100 g. Conversely, Sharples et al. (14) found that cerebral hyperemia was very uncommon. However, Sharples et al. (14) used a reference normal value of 65 mL/min/100 g (28). Close examination of the two studies (13, 14) shows that cerebral blood flow measurements in both studies were clustered around a mean of about 50 mL/min/100 g. The subsequent interpretations were mainly influenced by the choice of different reference values.

After severe head injury, the relationship between cerebral perfusion pressure and cerebral blood flow is altered and probably varies widely in different children. However, if autoregulation remains intact and $Paco_2$ is constant, it is likely that an increase in cerebral perfusion pressure will cause a small increase in cerebral blood flow (33), as long as cerebral perfusion pressure is above the lower limit of autoregulation (34). As we reduced $Paco_2$, intracranial pressure decreased in every case. Since mean arterial pressure remained constant, this decrease in intracranial pressure produced an increase in cerebral perfusion pressure over the course of each study. However, in almost all cases, cerebral blood flow decreased predictably after hyperventilation (Fig. 5). The negative effect of hypocarbic vasoconstriction on cerebral blood flow appeared to outweigh

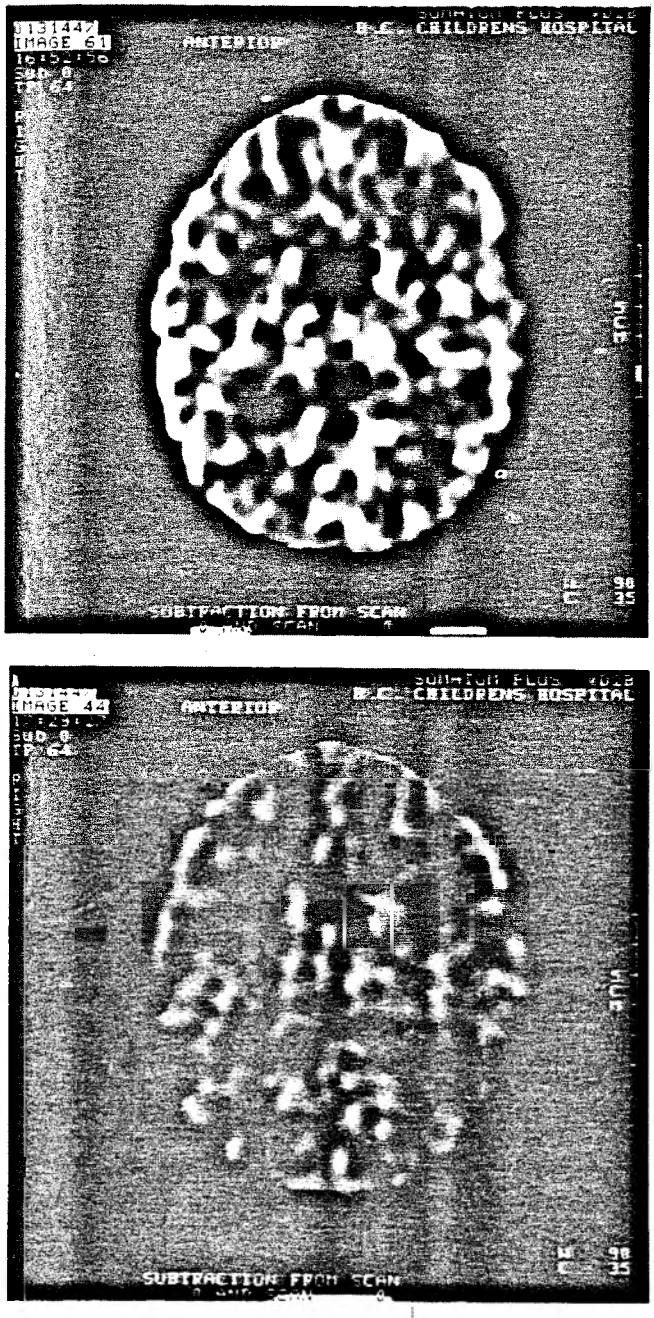

Figure 6. Xenon-enhanced computed tomography flow images from a child 16 hrs after a motor vehicle accident. Admission Glasgow Coma Scale was 5. *Top:* Scan performed at $Paco_2$ of 45 torr (6.0 kPa), intracranial pressure of 44 mm Hg, cerebral perfusion pressure of 54 mm Hg, and global cerebral blood flow of 59 mL/min/100 g. *Bottom:* Scan at same level, 15 mins after hyperventilation, shows clinically important cerebral ischemia. Scan performed at $Paco_2$ of 30 torr (4.0 kPa), intracranial pressure of 15 mm Hg, cerebral perfusion pressure of 82 mm Hg, and global cerebral blood flow of 14 mL/min/100 g. (Several local areas of this scan had regional cerebral blood flow rates of <10 mL/min/100 g.)

the small increase that might have been expected from the increase in cerebral perfusion pressure.

The relationship between cerebral perfusion pressure and cerebral blood flow and their ultimate effect on intracranial pressure is complex and cannot be adequately characterized without a measure of cerebral blood volume. Although we did not calculate cerebral blood volume in this study, we found no evidence to support the original claim by Bruce et al. (11) that cerebral hyperemia is common in head-injured children or that hyperemia is a major contributor to increased intracranial pressure in the first few days after injury. Our patients' blood flow rates were close to those rates found in previous studies (13, 14), and were clustered in the lower range of normal cited by Settergren et al. (28), with a mean of 49.6 ± 14.6 mL/min/100 g. Absolute cerebral hyperemia was rare at any time after head injury. In addition, there was no correlation between cerebral blood flow and intracranial pressure, which might have been expected if vascular engorgement were a major contributor to increased intracranial pressure.

Our patients showed a profound decrease in $CMRO_2$ after head injury. The group's mean value of 1.02 ± 0.59 mL/min/100 g was only a third of the normal value measured in anesthetized children (28). Although the cerebral blood flow rate was usually within the low normal range, this mean value still represented luxury perfusion because the measured blood flow rates were well above the metabolic requirements of most children. Both Muizelaar et al. (13) and Sharples et al. (14) noted a decrease in $CMRO_2$, but only to a level of about 2 mL/min/100 g. Muizelaar et al. (13) considered a $CMRO_2$ of <1.0 mL/min/100 g to be a reliable indicator of death. It is our unit's policy to avoid paralysis whenever possible. Consequently, all head-injured children are deeply sedated with morphine and midazolam infusions. This drug combination has been shown to reduce $CMRO_2$ by 25% (35) and probably contributed to the low values. However, our measured values of $CMRO_2$ are so much lower than previous studies that this observation requires further investigation.

Xenon-enhanced CT scanning has been shown to be a safe and accurate technique (6, 9). It provides visual and quantitative information about regional and global cerebral blood flow rates. However, the measurement of $C(a\text{-}j)O_2$ and subsequent calculations of $CMRO_2$ are open to considerable criticism. Cerebral venous drainage is not equally divided between the two jugular veins. Consequently, unilateral samples may not be a fair representation of the brain's metabolism (36). In addition, cerebral venous blood is diluted by flow from small emissary veins draining the face and scalp directly into the jugular bulb (29). When performed carefully, monitoring of jugular venous bulb oxygen saturation and calculation of the cerebral oxygen

extraction ratio have been shown to provide useful information (5, 25). The results should always be interpreted with caution because they can only represent an average value for the whole brain and provide no information on regional metabolism. Our venous sampling technique did not differ significantly from earlier studies and is not likely to be the explanation for the large difference between our measured values of $CMRO_2$ and earlier reports.

Controlled ventilation of patients with severe head injury has been accepted as the standard of care since 1971, when Gordon (19) demonstrated a more favorable outcome after intubation and hyperventilation. The assumption of benefit from hyperventilation has recently been challenged by several studies (17, 21). Our finding of a clear relationship between regional cerebral ischemia and hypocarbia supports the concerns raised in the pediatric literature that unmonitored hyperventilation in children with an acute brain injury may result in potentially dangerous reductions in cerebral blood flow (14). We agree with current adult recommendations (22) that hyperventilation should not be used as a routine therapy for patients of any age after a severe head injury.

Our approach to head-injury management produced results that are comparable with any in the literature. Good or moderate outcomes occurred in 52.2% of our patients, and the overall death rate was 4.3%. Although care for each child will inevitably vary, we believe that the basis of head-injury management should be obsessive attention to oxygenation and cerebral perfusion pressure, combined with core temperature and metabolic homeostasis (particularly control of serum concentrations of glucose and sodium). We also advocate careful monitoring of minute ventilation and end-tidal CO_2 levels to try and avoid episodes of inadvertent hyperventilation that can easily occur during patient transport. Additional therapies should only be added after careful prospective study.

Hyperventilation should be reserved as a last resort for the control of increased intracranial pressure and, whenever possible, should be monitored by calculation of the cerebral oxygen extraction ratio using a jugular venous bulb catheter and, ideally, a xenon-enhanced CT flow study. Hyperventilation has a part to play in the management of children with head injuries. However, hyperventilation should be used with caution and monitored carefully.

ACKNOWLEDGMENT

We thank Mr. Dale Northy of the Department of Biomedical Communications for his careful preparation of the illustrations.

REFERENCES

1. Souter M, Andrews P: A review of jugular venous oximetry. *Intensive Care World* 1996; 13:32–38
2. Ritter A, Robertson C: Cerebral metabolism. *Neurosurg Clin N Am* 1994; 5: 633–645
3. Obrist W, Langfitt T, Jaggi J, et al: Cerebral blood flow and metabolism in comatose patients with acute head injury. *J Neurosurg* 1984; 61:241–253
4. Bruce D, Langfitt T, Miller J, et al: Regional cerebral blood flow, intracranial pressure and brain metabolism in comatose patients. *J Neurosurg* 1973; 38:131–144
5. Robertson C, Narayan R, Gokaslan Z, et al: Cerebral arteriovenous oxygen difference as an estimate of cerebral blood flow in comatose patients. *J Neurosurg* 1989; 70:222–230
6. Stringer W, Hasso A, Thompson J, et al: Hyperventilation-induced cerebral ischemia in patients with acute brain lesions: Demonstration by xenon-enhanced CT. *Am J Neuroradiol* 1993; 14:475–484
7. Graham D, Ford I, Hume-Adams J, et al: Ischaemic brain damage is still common in fatal non-missile head injury. *J Neurol Neurosurg Psychiatry* 1989; 52:346–350
8. Bouma G, Muizelaar J, Choi S, et al: Cerebral circulation and metabolism after severe traumatic brain injury: The elusive role of ischemia. *J Neurosurg* 1991; 75:685–693
9. Bouma G, Muizelaar J, Stringer W, et al: Ultra-early evaluation of regional cerebral blood flow in severely head-injured patients using xenon-enhanced computerized tomography. *J Neurosurg* 1992; 77:360–368
10. Bruce D, Raphaely R, Goldberg A, et al: Pathophysiology, treatment and outcome following severe head injury in children. *Child's Brain* 1979; 5:174–191
11. Bruce D, Alavi A, Bilaniuk L, et al: Diffuse cerebral swelling following head injuries in children: The syndrome of "malignant brain edema." *J Neurosurg* 1981; 54:170–178
12. Hammer G, Lindsay J: The neurosurgical pediatric patient. *In:* Neurosurgical Intensive Care. Andrews B. (Ed). New York, McGraw-Hill, 1993
13. Muizelaar J, Marmarou A, DeSalles A, et al: Cerebral blood flow and metabolism in severely head-injured children. Part 1: Relationship with GCS score, outcome, ICP and PVI. *J Neurosurg* 1989; 71:63–71
14. Sharples P, Stuart A, Matthews D, et al: Cerebral blood flow and metabolism in children with severe head injury. Part 1: Relation to age, Glasgow Coma Score, outcome, intracranial pressure and time after injury. *J Neurol Neurosurg Psychiatry* 1995; 58: 145–152
15. Gleason C, Short B, Jones M: Cerebral blood flow and metabolism during and after prolonged hypocapnia in newborn lambs. *J Pediatr* 1989; 115:309–314
16. Muizelaar J, Van Der Poel H, Li Z, et al: Pial arteriolar vessel diameter and CO_2 reactivity during prolonged hyperventilation in the rabbit. *J Neurosurg* 1988; 69:923–927
17. Marion D, Bouma G: The use of stable xenon-enhanced computed tomographic studies of cerebral flood flow to define changes in cerebral carbon dioxide vasoresponsivity caused by a severe head injury. *Neurosurgery* 1991; 29: 869–873
18. Marion D, Darby J, Yonas H: Acute regional cerebral blood flow changes caused by severe head injuries. *J Neurosurg* 1991; 74:407–414
19. Gordon E: Controlled respiration in the management of patients with traumatic brain injuries. *Acta Anaesthesiol Scand* 1971; 15:193–208
20. Muizelaar J, Marmarou A, Ward J, et al: Adverse effects of prolonged hyperventilation in patients with severe head injury: A randomized clinical trial. *J Neurosurg* 1991; 75:731–739
21. Cold G: Does acute hyperventilation provoke cerebral oligemia in comatose patients after acute head injury? *Acta Neurochir* 1989; 96:100–106
22. Guidelines for the management of severe head injury. Washington, DC, Brain Trauma Foundation, July 1995, pp A5–A9
23. Rosner M, Rosner S, Johnson A: Cerebral perfusion pressure: Management protocol and clinical results. *J Neurosurg* 1995; 83:949–962
24. Gur D, Wolfson S Jr, Yonas H, et al: Progress in cerebrovascular disease: Local cerebral blood flow by xenon enhanced CT. *Stroke* 1982; 13:750–758
25. Gayle M, Frewen T, Armstrong R, et al: Jugular venous bulb catheterization in infants and children. *Crit Care Med* 1989; 17:385–388
26. Kennedy C, Sokoloff L: An adaptation of the nitrous oxide method to the study of the cerebral circulation in children; normal values for cerebral blood flow and cerebral metabolic rate in childhood. *J Clin Invest* 1957; 36:1130–1137

27. Lou H, Lasser N, Friis-Hansen B: Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *J Pediatr* 1979; 94:118–123
28. Settergren G, Lindblad B, Persson B: Cerebral blood flow and exchange of oxygen, glucose, ketone bodies, lactate, pyruvate and amino acids in anesthetised children. *Acta Paediatr Scand* 1980; 69:457–465
29. Kety S, Schmidt C: The nitrous oxide method for the quantitative determination of cerebral blood flow in man: Theory, procedure and normal values. *J Clin Invest* 1948; 27:476–483
30. Sharples P, Stuart A, Aynsley-Green A, et al: A practical method of serial bedside measurement of cerebral blood flow and metabolism during neurointensive care. *Arch Dis Child* 1991; 66:1326–1332
31. Astrup J: Energy-requiring cell functions in the ischaemic brain. Their critical supply and possible inhibition in protective therapy. *J Neurosurg* 1982; 56: 482–497
32. Jennett B, Bond M: Assessment of outcome after severe brain damage: A practical scale. *Lancet* 1975; i:480–484
33. Handa Y, Hayashi M, Takeuchi H, et al: Time course of the impairment of cerebral autoregulation during chronic cerebral vasospasm after subarachnoid hemorrhage in primates. *J Neurosurg* 1992; 76:493–501
34. Rosner M: Pathophysiology and management of increased intracranial pressure. *In:* Neurological Intensive Care. Andrews B (Ed). New York, McGraw-Hill, 1995, p 69
35. Stephan H, Sonntag H, Lange H, et al: Cerebral effects of anaesthesia and hypothermia. *Anaesthesia* 1989; 44:310–316
36. Stocchetti N, Paparella A, Bridelli F, et al: Cerebral venous oxygen saturation studied with bilateral samples in the internal jugular veins. *Neurosurgery* 1994; 34:38–44
37. Eisenberg H, Gary H, Aldrich E, et al: Initial CT findings in 753 patients with severe head injury: A report from the NIH traumatic coma data bank. *J Neurosurg* 1990; 73:688–698

Appendix. Equations

$$CMRO_2 = C(a\text{-}j)O_2 \times CBF \quad [1]$$

$$C(a\text{-}j)O_2 = 1.34 \times Hb(Sao_2 - SJVo_2) + 0.003(Pao_2 - Pvo_2) \quad [2]$$

$$CPP = MAP - ICP \quad [3]$$

$$CO_2R = \frac{100 \times \frac{(CBF_i - CBF_f)}{CBF_f}}{(Paco_{2i} - Paco_{2f})} \quad [4]$$

$$OER = \frac{Sao_2 - SJVo_2}{Sao_2} \times 100 \quad [5]$$

$CMRO_2$, cerebral metabolic rate of oxygen consumption; $C(a\text{-}j)O_2$, arterial-jugular venous oxygen content difference; CBF, cerebral blood flow; Hb, hemoglobin; SaO_2, arterial oxygen saturation; $SJVO_2$, jugular venous bulb oxygen saturation; PvO_2, venous partial pressure of oxygen; CPP, cerebral perfusion pressure; MAP, mean arterial pressure; ICP, intracranial pressure; CO_2R, CO_2 vasoreactivity; CBF_i, initial value of cerebral blood flow; CBF_f, final value of cerebral blood flow; $PaCO_{2i}$, initial arterial partial pressure of CO_2; $PaCO_{2f}$, final arterial partial pressure of CO_2.